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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/766,500 01/19/01 RUECKER

C 2997-19

EXAMINER

HM12/1105

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DAVIS,R	ART UNIT	PAPER NUMBER
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1651

DATE MAILED:

11/05/01

H.A.

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/766,500	RUECKER ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 August 2001.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) 20-46 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-19 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1 – 19 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that the inventions of Groups II and III overlap such that the search of Group I would include subject matter of Groups II and III. This is not found persuasive because an overlapping search is not a coextensive search. Moreover, the inventions have acquired a separate status in the art as a separate subject for inventive effect and require independent searches (as indicated by the different classification). The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 – 6 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Gudin et al. (US 5179012).

Applicant claims a process for obtaining lipid from microorganisms comprising lysing cells of the microorganism, treating the lysed cells to produce a heavy layer of an aqueous solution and a light layer of lipid, separating the layers from each other and obtaining the lipid form the light layer, wherein the microorganism is selected from algae, fungi, bacteria or protist and the step of treating the lysed cells comprises centrifuging. Specifically, the lipid is emulsified and comprises a suspension of lipid in an aqueous solution and the aqueous solution comprises solid cell material. The process further comprises adding an aqueous extraction solution to the light layer until the lipid is substantially non-emulsified.

Gudin et al. teach a process which produces lipids wherein microalgae are cultured, dissolved, crushed (or lysed) and treated to produce separate layers, whereby the layers are separated (col.2 line 37-55) into two phases: a lipid solution and an aqueous solution containing cellular residues (or solid cell material) wherein the treatment (or separation) is carried out via centrifuging (col.4 line 11-20). Gudin et al. further teach that the lipid phase can be further concentrated and/or purified by ultrafiltration or precipitation with ammonium sulfate (or an aqueous extraction solution) (col.4 line 24-30).

Although Gudin et al. do not specifically teach an emulsified lipid in solution whereby it becomes substantially non emulsified, Gudin et al. do teach a lipid solution whereby the lipid is precipitated out col.4 line 20-30). At the time of the invention, it was known in the art that a lipid in solution is substantially an emulsified lipid and that by precipitating out the lipid (in this case with an aqueous extraction solution ammonium sulphate), the lipid becomes substantially non-emulsified.

Therefore, the reference anticipates the claimed subject matter.

Art Unit: 1651

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 7 – 10 and 12 – 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gudin et al. (US 5179012) in view of Barclay (US 5130242).

Applicant claims a process for obtaining lipid from microorganisms comprising lysing cells of the microorganism, treating the lysed cells to produce a heavy layer of an aqueous solution and a light layer of lipid, separating the layers from each other and obtaining the lipid from the light layer. The microorganism is selected from algae, fungi, bacteria or protist, specifically from the order Thraustochytriales, genus Thraustochytrium, Schizochytrium or mixtures thereof. More specifically, they are selected from microorganism with identifying characteristics of ATCC 20888, 20889, 20890, 20891, 20892, mutants thereof or combinations thereof. The microorganism is capable of growth at salinity levels of less than about 12 g/L of

Art Unit: 1651

sodium chloride, capable of producing at least about 0.1 g/L/hour of docosahexaenoic acid (DHA) and comprises at least about 30% by weight of lipid, wherein at least about 30% of said lipid is DHA. Finally, the microorganisms are obtained from a fermentation process whereby a base selected from hydroxides, carbonated, bicarbonates or mixtures thereof is added to the fermentation broth and at least part of proteinaceous compounds are solubilized in the fermentation broth.

Gudin et al. teach a process which produces lipids wherein microalgae are cultured, dissolved, crushed (or lysed) and treated to produce separate layers, whereby the layers are separated (col.2 line 37-55) into two phases whereby the lipid phase can be further concentrated and/or purified by ultrafiltration or precipitation (col.4 line 24-30).

Gudin et al. do not teach the process wherein the microalgae are from the order Thraustochytriales, genera Thraustochytrium, Schizochytrium, mixtures thereof, or microorganisms with identifying characteristics of ATCC 20888, 20889, 20890, 20891, 20892, mutants and/or combinations thereof obtained from a fermentation process. However, at the time of the invention, one of ordinary skill in the art would have been motivated to do so because Barclay teaches a process for the production of microbial products with high concentration of omega 3 highly unsaturated fatty acids, or omega-3 HUFAs, (lipids) using microorganisms of the order Thraustochytriales (abstract). Specifically, Barclay teaches the process wherein Thraustochytrium, Schizochytrium or mixtures thereof are cultured to produce high concentrations of omega-3 HUFAs (col.5 line 20-35). In addition, microorganisms with identifying characteristics of ATCC 20888, 20889, 20890, 20891, 20892 and mutants therefrom

Art Unit: 1651

are utilized (col.5 line 45-50). Barclay teaches that such microorganisms are fermented with grain to produce the desired omega-3 HUFAs (col.8 line 50-60).

Gudin et al. do not teach the process wherein the fermentation broth comprises solubilized proteinaceous compounds. However, at the time of the invention, one of ordinary skill in the art would have been motivated to do so because Barclay teaches that biomass comprised of proteins and carbohydrates can be recycled into the fermentor whereby it acts as a nutrient source for the *Thraustochytrium* (col.14 line 34-45). Although Barclay does not specifically teach solubilizing the proteins, at the time of the invention, one of ordinary skill in the art would have recognized that by mixing the proteinaceous compounds back into the fermentation broth, the material would become solubilized. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by Barclay to solubilize proteinaceous compounds in the fermentation broth as a source of nutrients for the microorganism with a reasonable expectation of success for obtaining lipids from a microorganism.

The above references do not specifically teach the process wherein the microorganism comprises at least about 30% by weight of the lipid, are capable of producing at least about 0.1 g/L/hour of docosahexaenoic acid (DHA), wherein at least about 30% of the lipid is DHA or wherein the microorganism is capable of growth at salinity levels of less than about 12 g/L of sodium chloride. However, Barclay does teach desirable characteristics of microorganisms include high content of omega-3 HUFAs and that they are euryhaline, or able to grow in a wide range of salinity, especially a low salinity (col.6 line 42-54). In addition, Barclay names omega-3 HUFAs to include docosahexaenoic acid, of DHA (col.6 line12-38). At the time of the

Art Unit: 1651

invention, one of ordinary skill in the art would have been motivated by Barclay to utilize a microorganism with the instantly claimed characteristics because Barclay teaches such characteristics are economically desirable for the production of omega-3 HUFAs (col.6 line 43-47). Furthermore, at the time of the invention, one of ordinary skill in the art would have been able to recognize that optimizations of such characteristics would be desirable in a process for obtaining lipids, as demonstrated and suggested by Barclay.

The above references do not specifically teach adding a base selected from hydroxides, carbonates, bicarbonates or mixtures thereof. However, Barclay teaches that growth of the instant strains by the instant process typically becomes more alkaline during fermentation and prefer the range of pH 5.5 – 8.5 (col.9 line 34-41). At the time of the invention, one of ordinary skill in the art would have been motivated by Barclay to add a base to the fermentation broth because of the disclosed range of pH 5.5 – 8.5 that is preferred for growth. Furthermore, it would have been obvious to one of ordinary skill in the art to utilize hydroxides, carbonates, bicarbonates or mixtures thereof because they were well known bases used in the art at the time the invention was made. In support, Wagner et al. (US 4720456) teach isolation of lipids from a fermentation broth wherein the pH of the culture medium is adjusted to pH 3 – 8 by addition of alkaline compounds (or bases) (col.4 line 44-57) to include sodium hydroxide (example 9).

7. Claims 1, 7 – 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gudin et al. (US 5179012) in view of Wagner et al. (US 4720456).

Applicant claims a process for obtaining lipid from microorganisms comprising lysing cells of the microorganism, treating the lysed cells to produce a heavy layer of an aqueous solution

Art Unit: 1651

and a light layer of lipid, separating the layers from each other and obtaining the lipid form the light layer wherein the microorganisms are obtained from a fermentation process wherein a base selected from hydroxides, carbonated, bicarbonates or mixtures thereof is added to the fermentation broth. The step of lysing said cells comprises heating the microorganisms to at least about 50C.

Gudin et al. teach a process which produces lipids wherein microalgae are cultured, dissolved, crushed (or lysed) and treated to produce separate layers, whereby the layers are separated (col.2 line 37-55) into two phases whereby the lipid phase can be further concentrated and/or purified by ultrafiltration or precipitation (col.4 line 24-30).

Gudin et al. do not teach the process wherein the microorganisms are obtained from a fermentation broth wherein a base selected from hydroxides, carbonates, bicarbonates, or mixtures thereof are added to the broth. However, Wagner et al. teach a process for isolation of lipids from microorganisms obtained from a fermentation broth wherein pH of the culture medium is adjusted to pH 3 – 8 by addition of alkaline compounds (or bases) (col.4 line 44-57) to include sodium hydroxide (example 9). At the time of the invention, one of ordinary skill in the art would have been motivated to obtain the microorganisms of Gudin et al. by fermentation with added bases because it was well known in the art to do so in methods for obtaining lipids from microorganisms, as demonstrated by Wagner et al. Furthermore, it would have been obvious to utilize any of the instant bases as they were well known and used bases in the art at the time the invention was made. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by routine practice to include bases in the fermentation broth

Art Unit: 1651

of Gudin et al. with a reasonable expectation of success for obtaining lipids from microorganisms.

Gudin et al. do not teach the process wherein heating the microorganism to about 50C lyses the cells. However, Wagner et al. teach that the growth of the cells are terminated by a temperature increase to about 60C (col.1 line 19-22). Although Wagner et al. do not specifically teach that this temperature shock lyses the cells, at the time of the invention, one of ordinary skill in the art would have recognized that such a step would achieve this effect. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated to heat the cells to at least about 50C with a reasonable expectation of success for terminating cell growth, or lysing the cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
November 2, 2001


LEON B. LANKFORD, JR.
PRIMARY EXAMINER